Contemporary outcomes for surgical mitral valve repair: A benchmark for evaluating emerging mitral valve technology

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Objective: The emergence of transcatheter approaches to mitral valve (MV) repair has focused attention on outcomes after surgical MV repair. Results from the EVEREST II trial demonstrated worse short-term major adverse event (MAE) rates for surgical repair. This study analyzes contemporary outcomes of surgical MV repair to establish a benchmark for future therapeutic comparisons.

Methods: From 2003 to 2008, 903 isolated MV repair operations were performed at 13 different statewide cardiac centers. Patients were excluded if they had prior valve operations or mitral stenosis similar to EVEREST II. MAE rate was defined using similar criteria to EVEREST II, including postoperative atrial fibrillation and transfusion of 2 units of blood or more. Univariate analyses and multivariate regression models were applied to identify independent predictors of MAEs after surgical MV repair.

Results: Mean patient age was 57.0 ± 13.2 years, and the majority of patients were men (59.0%, 533/903). The prevalence of preoperative risk factors was as follows: stroke 3.9% (35/903), immunosuppression 2.4% (22/903), heart failure 32.1% (290/903), renal failure 3.5% (32/903), and previous coronary artery bypass grafting 3.4% (31/903). Mean ejection fraction was 55.6 ± 11.3%. MAE rate was 29.0% (262/903), including atrial fibrillation 17.6% (159/903), renal failure 1.3% (12/903), stroke 0.9% (8/903), and operative mortality 1.1% (10/903). Multivariate correlates of MAE included the following: advanced age, prior stroke, immunosuppression, and operation time. Importantly, gender, previous coronary bypass grafting, renal failure, and ejection fraction were not independent predictors of MAE.

Conclusions: In the current era, patients undergoing surgical MV repair have low mortality. MAE rate was largely due to postoperative atrial fibrillation. These results may help to stratify which patients may be best served with newer technologies. (J Thorac Cardiovasc Surg 2012;143:S12-6)

It is generally accepted that mitral valve (MV) repair is the preferred surgical approach for patients with severe mitral regurgitation (MR).[1-4] MV repair has several intrinsic advantages over bioprosthetic or mechanical valve replacement, and the efficacy of MV repair has been demonstrated for both degenerative and ischemic MV etiology.[5,6]

The recent emergence of transcatheter approaches to MV repair has extended treatment options for patients with significant MR. However, the durability of such approaches has yet to be widely established. In the recently published EVEREST II trial, 279 patients were randomly assigned in a 2:1 ratio to receive either percutaneous or surgical treatment for 3 to 4+ mitral insufficiency.[7] The goal of the trial was to determine the safety and efficacy of each treatment approach by examining differences in composite end points. In the assessment of safety, the primary end point was the composite incidence of major adverse events (MAEs), and the authors reported improved safety for percutaneous repair with an MAE rate of 15% compared with 48% with surgical treatment. However, criticism of these comparisons has arisen owing to the large influence that packed red blood cell (PRBC) transfusion rates exerted on the MAE composite end point, and when transfusion rates were not considered in the MAE analysis, no significant differences existed in safety between percutaneous and surgical treatment.

In light of these reported results, the objective of this study was to examine contemporary outcomes for surgical MV repair within a multi-institutional cohort of patients to establish a more accurate benchmark for future therapeutic comparisons.

PATIENTS AND METHODS

Patients

This study was exempt from University of Virginia Institutional Review Board review. Deidentified patient records were obtained from the Virginia

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Abbreviations and Acronyms

CI = confidence interval
MAE = major adverse event
MR = mitral regurgitation
MV = mitral valve
OR = odds ratio
PRBC = packed red blood cell
STS = The Society of Thoracic Surgeons
VCSQI = Virginia Cardiac Surgery Quality Initiative (database)

Cardiac Surgery Quality Initiative (VCSQI) database. The VCSQI is a voluntary consortium of 16 different statewide cardiac centers that captures approximately 99% of all cardiac procedures within the commonwealth of Virginia. Each VCSQI center contributes its data to The Society of Thoracic Surgeons (STS) Adult Cardiac Database. This secondary analysis of the VCSQI database retrospectively reviewed all patients undergoing isolated MV repair procedures from January 2003 to December 2008. To provide a similar estimate of outcomes to those reported in the EVEREST II trial, we excluded patients with rheumatic heart disease, mitral stenosis, and prior endocarditis.

Patient risk factors, operative features, postoperative complications, and total hospital length of stay were evaluated. Established STS definitions for all analyzed variables were used. Operative mortality included patient deaths that occurred before hospital discharge or within 30 days of operation. Similar to EVEREST II, the composite outcome of MAEs included the following: death, stroke, reoperation for valve dysfunction, urgent/emergency reoperation, perioperative myocardial infarction, renal failure, deep sternal wound infection, prolonged mechanical ventilation (>24 hours), new-onset atrial fibrillation, sepsis, gastrointestinal complication, and total (intraoperative and postoperative) transfusion of 2 units of PRBCs or more.

Statistical Analysis

The primary outcomes of interest were MAE rate and the identification of independent predictors of MAE. Secondary outcomes included the incidence of individual postoperative complications, operative mortality, and postoperative length of stay. Continuous variables are reported as mean $\pm$ standard deviation, and categorical variables are expressed as percentage of the total study population. Univariate analyses for the outcome of MAE included χ^2 or Fisher's exact test for categorical variable comparisons, whereas single-factor analysis of variance was used to compare continuous data.

Multiple logistic regression was used to identify independent predictors of MAE after adjusting for the confounding influence of various patient- and operation-related risk factors. All preoperative variables entered as covariates were selected a priori on the basis of established clinical risk for MV operations. Odds ratios (ORs) with a 95% confidence interval (CI) are used to report the results of logistic regression modeling. Model performance was assessed by the Hosmer-Lemeshow goodness of fit test and by evaluating the area under the receiver operating characteristics curve. Reported P values are 2-tailed. Data manipulation and analysis were performed using Predictive Analytics SoftWare, version 18 (IBM Corporation, Somers, NY).

RESULTS

Patient Characteristics and Operative Features

A total of 903 patients underwent MV repair and met study inclusion and exclusion criteria during the 5-year study period. The overall MV repair rate for all study centers was 53.3% during the study period, and the rate of MV repair differed as a function of hospital procedure volume. MV repair rate was 65.9% for the highest volume center during the study period and 29.6% for the lowest volume center during the study period. Mean patient age was 57 years, and women accounted for 41.0% of all patients. The prevalence of major comorbid disease included stroke (3.9%), diabetes (9.1%), heart failure (32.1%), and renal failure (3.5%). Mean ejection fraction was 55.6%. Moderate (12.5%) and severe (81.7%) MR accounted for the majority of cases. Previous coronary artery bypass grafting occurred in 3.4% of patients. The majority of cases were elective MV repair (85.2%) and consisted of MV reconstruction with annuloplasty (68.9%).

Incidence of Postoperative Outcomes After Surgical MV Repair

The most common postoperative complications (Figure 1) included atrial fibrillation (17.6%), transfusion of 2 units of PRBCs or more (8.6%), prolonged mechanical ventilation (4.5%), reoperation for bleeding/tamponade (3.5%), and renal failure (1.3%). Operative mortality was 1.1%. The composite MAE rate was 29.0% and decreased to 13.8% when the influence of postoperative atrial fibrillation was removed. The average postoperative length of stay was 6.1 $\pm$ 4.6 days.

Univariate and Multivariate Correlates of MAEs

To identify univariate correlates of MAEs, we stratified patient data by the outcome of MAE. Patient factors found to be significantly associated with the incidence of MAE included the following: increased patient age ($P < .001$), female gender ($P = .04$), presence of cerebrovascular disease ($P = .002$), preoperative stroke ($P < .001$), immunosuppressive therapy use ($P < .001$), history of angina ($P = .02$), heart failure ($P < .001$), preoperative arrhythmia ($P < .001$), advanced New York Heart Association class ($P < .001$), renal failure ($P = .02$), and declining ejection fraction ($P = .004$). The performance of urgent/emergency operations ($P < .001$) as well as MV repair with either annuloplasty alone ($P < .001$) or an MV reconstruction without annuloplasty ($P < .001$) were significant operation-related correlates of MAE. On multiple logistic regression (Table 1), only patient age, preoperative stroke, and immunosuppressive therapy use were statistically associated with the composite MAE outcome. Importantly, female gender, renal failure, history of coronary artery bypass grafting, and preoperative ejection fraction had no significant association with MAE. The predictive model proved to be an adequate performer with a Hosmer-Lemeshow $P = .07$ and an area under the curve = 0.82.

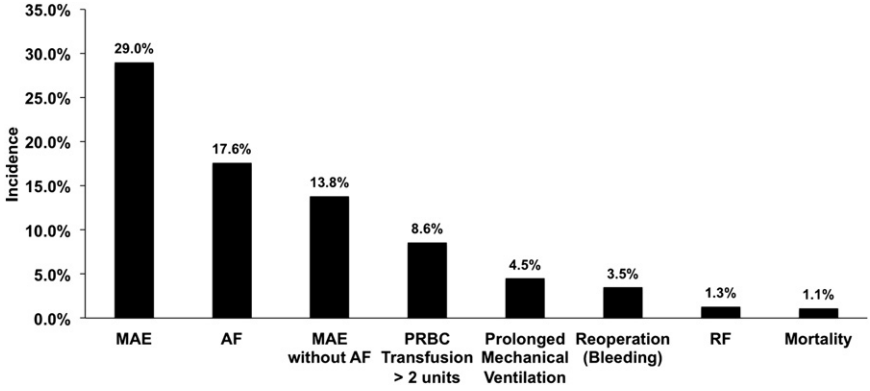

FIGURE 1. Incidence of postoperative complications. *MAE*, Major adverse event rate; *AF*, atrial fibrillation; *PRBC*, packed red blood cells; *RF*, renal failure.

COMMENT

The present study provides a generalizable report of contemporary postoperative outcomes after surgical MV repair within a multi-institutional cohort of 903 patients who were operated on by both high- and low-volume mitral surgeons at 16 different statewide centers. Despite surgeon volumes, however, surgical MV repair was associated with low operative mortality and acceptable morbidity. Using similar inclusion and exclusion criteria to that of the EVEREST II trial, we have provided an alternative report of postoperative outcomes to establish a benchmark on which to base future therapeutic comparisons. The definition of MAE rate in the present report is similar to that used in EVEREST II. However, the composite incidence of MAE is this series (29%) proved to be substantially lower than that reported for the surgical arm in EVEREST II (48%). More important, postoperative atrial fibrillation largely influenced the incidence of MAE in our series. In addition, we identified important univariate and multivariate correlates of MAE to further identify at-risk patient populations undergoing surgical MV repair, including advanced patient age, stroke, and preoperative immunosuppressive therapy use. These results not only serve to provide a generalizable report of current MV repair outcomes but also extend the discussion of important discrepancies that may exist between investigations designed to assess the comparative effectiveness of emerging MV repair technology.

TABLE 1. Multivariable logistic regression results for the outcome of MAEs among patients undergoing isolated MV repair operations (n = 903)

Covariate	OR	95% CI	*P* value
Age	1.046	1.029-1.063	**<.001**
Stroke	3.206	1.244-8.263	**.02**
Immunosuppressive therapy	9.958	2.286-43.379	**.002**
Gender (female)	1.266	0.875-1.830	.21
Peripheral vascular disease	0.712	0.273-1.860	.49
Diabetes	0.733	0.371-1.449	.37
Dyslipidemia	1.029	0.695-1.523	.89
Hypertension	1.022	0.707-1.478	.91
Renal failure	0.896	0.123-6.556	.91
Hemodialysis	1.800	0.164-19.751	.63
Previous CABG	0.983	0.298-3.247	.98
Angina	1.801	0.856-3.789	.12
Arrhythmia	0.757	0.411-1.394	.37
NYHA III	1.234	0.806-1.889	.33
NYHA IV	1.512	0.548-4.175	.43
Heart failure	1.063	0.681-1.660	.79
Urgent/emergency status	0.000	0.000-0.000	.99
IABP	4.228	0.332-53.900	.27
Ejection fraction (%)	0.985	0.968-1.003	.1

Model performance: Area under receiver operator curve = 0.82. *P* values in bold are statistically significant. *MAE*, Major adverse event; *MV*, mitral valve; *OR*, odds ratio; *CI*, confidence interval; *CABG*, coronary artery bypass grafting; *NHYA*, New York Heart Association; *IABP*, intra-aortic balloon pump.

The results of the present study are in agreement with other recent surgical series. The 1.1% operative mortality rate compares favorably with nationwide mortality rates for MV repair of approximately 1.4% to 1.5%.[8,9] In addition, we report a slightly lower incidence of need for reoperation, postoperative stroke rates, and new-onset hemodialysis requirements compared with other recent estimates.[9] The average postoperative length of stay of 6 days after MV repair is also similar to that reported by Gammie and colleagues[9] in their recent review of nationwide outcomes. Perhaps even more important, however, is that these outcomes compare favorably with recently reported results comparing percutaneous MV repair with surgical repair or replacement.

Earlier this year, Feldman and colleagues[7] published the results of the EVEREST II trial and reported improved safety of percutaneous repair. In their analysis, MAE occurred in 15% of percutaneously treated patients compared with 48% of surgically treated patients. Important to consider in these results was the inclusion of both MV repair and replacement operations in the surgical arm of this trial and the fact that worse outcomes after MV replacement have been well documented in prior studies.[2,3,6]

TABLE 2. MAE rate for percutaneous and surgical arms of EVEREST II and surgical MV repair in the present series

MAE	EVEREST II		
	Percutaneous arm	Surgical arm	Surgical MV repair
Overall	9.6%	57.0%	29.0%
Death	0.0%	2.5%	1.1%
Myocardial infarction	0.0%	0.0%	0.0%
Reoperation for surgical failure	0.0%	1.3%	0.0%
Urgent or emergency surgery for adverse event*	0.0%	5.1%	3.5%
Stroke	0.0%	2.5%	0.0%
Renal failure	0.0%	0.0%	1.3%
Deep wound infection	0.0%	0.0%	0.0%
Prolonged ventilation†	0.0%	5.1%	4.5%
GI complication	0.7%	0.0%	0.0%
Atrial fibrillation‡	0.0%	0.0%	17.6%
Sepsis	0.0%	0.0%	0.0%
Transfusion >2 units of blood	8.8%	53.2%	8.6%

MAE, Major adverse event; *MV*, mitral valve; *GI*, gastrointestinal. *Rate of reoperation for bleeding for surgical MV repair patients. †Prolonged ventilation (mechanical ventilation >48 hours for EVEREST II and >24 hours for surgical MV repair). ‡Atrial fibrillation: New onset of persistent atrial fibrillation for EVEREST II.

Furthermore, in the overall assessment of the composite incidence of MAE in EVEREST II, the disproportionate outcomes between the percutaneous and surgical arms was largely influenced by the higher rate of PRBC transfusion after surgical treatment. As a result, once this factor was eliminated from analysis, the composite MAEs were no longer significantly different between percutaneous and surgical treatment of mitral insufficiency.

In light of these findings, the most significant results of the present study were the significantly lower composite MAE rate for isolated, surgical MV repair (29.0%) compared with that reported in the surgical arm of EVEREST II (Table 2). Other striking differences between the present series and that reported in EVEREST II were the significantly lower total PRBC transfusion rate (8.6%), stroke rate (0.9%), reoperation rate for valve dysfunction (0.3%), and mortality rate (1.1%). Unlike that observed in EVEREST II, we noticed that the composite MAE rate in this series was largely influenced by postoperative atrial fibrillation and not dominated by transfusion differences. This is likely due to a difference in definition of atrial fibrillation. EVEREST II reported the incidence of permanent atrial fibrillation, whereas in our series atrial fibrillation used the STS definition, which is simply the presence of new-onset postoperative atrial fibrillation irrespective of persistent atrial fibrillation. When we removed this complication from the analysis of MAE, the composite incidence dropped to 13.8%. In the present series the 8.6% rate of significant PRBC transfusion included both intraoperative and postoperative transfusions, which may explain the discordance with the lower incidence for reoperation for bleeding (3.5%). More important, however, the incidence of major transfusion was much lower than that reported for the surgical arm in EVEREST II (53.2%) and compares favorably with the 8.8% rate for the percutaneous arm.

To further stratify which patients may be more or less likely to encounter MAE after surgical MV repair, we identified patient- and operation-related factors that had significant univariate and multivariate associations with the onset of MAE. As a result, advanced patient age by year was associated with a 4.6% increase in the odds of encountering an MAE after surgical MV repair, whereas preoperative stroke and history of immunosuppressive therapy were associated with a 3.2-fold and 9.9-fold increase in the odds of MAE. These results are important in an era of increasing emphasis on individual patient risk stratification and suggest that patients with these risk factors should be considered for novel MV therapies if they prove durable.

This study has limitations. The retrospective study design introduces inherent selection bias, while the influence of surgeon selection for MV repair versus replacement cannot be accounted for and may have influenced the reported results. The use of established STS definitions for all examined variables, differences in the definitions of certain adverse events (ie, prolonged ventilation, postoperative atrial fibrillation), as well as the presence of completely deidentified data limited the ability to provide exact comparisons with other trials, including the EVEREST II. In addition, the reported results may not be extrapolated to MV replacement outcomes and may, thus, be of limited utility to centers with low MV repair rates. Certain data, including valve morphology or etiology, could not be analyzed, and long-term follow-up would add impact to the reported results. Nevertheless, the markedly improved outcomes after MV repair reported in this series provide an important clinical contribution inasmuch as they highlight contemporary trends within a multi-institutional cohort of patients that are highly generalizable to patients undergoing treatment for moderate to severe mitral insufficiency.

CONCLUSIONS

On the basis of the reported results, patients undergoing surgical MV repair have low mortality and acceptable morbidity. Composite MAE rate was largely influenced by postoperative atrial fibrillation. These results compare favorably with recently reported trials examining both percutaneous and surgical treatment approaches to mitral insufficiency and may help to stratify which patients may be best served with newer technologies.

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